REMARKS

Claims 1-8 and 18-20 are currently cancelled herein.

The paragraphs located at page 3, lines 44-52, page 5, lines 40-48, and page 7, lines 32-52 have now been replaced with identical paragraphs for legibility. Please enter these replacement paragraphs.

The various items as numbered in the Action are addressed below.

Item 1. Three regions of the disclosure stand objected for containing unreadable copy: page 3, lines 45-52; page 5, lines 40-48; and page 7 lines 40-47. These three regions have now been amended by submission of replacement paragraphs. Applicants believe that these amendments overcome the objection and respectfully request that it be removed.

Items 1-2. No remarks are required.

Item 3. Applicants recognize the duty under 37 CFR 1.56 to point out the required information for subject matter not commonly owned. . . . Applicants believe that all subject matter hereof was and remains commonly owned. . . .

Items 4, 5, and 7. Claims 1-8 and 18-20 stand rejected for alleged obviousness over various references (Chappell et al., Chappell et al. in view of Waggle et al.; or presumably over or in light of Kipriyanova et al. [Derwent 1994-107916]). The cited teachings of these references are that it is known that aqueous isopropanol can be used to make extracts and that chromatography of such extracts has been performed. However, this combination does not teach or suggest the present invention (*including* Claims 1-9 and 18-20).

The teachings of these references are limited to extractions of a single species or a narrow species group of hydrophobic hydrocarbon alcohols: sterols in Chappell et al. and Waggle et al.; and retinol in Kipriyanova et al. Moreover, Chappell et al. teach that any of a wide variety of hydrophilic and hydrophobic solvents and solvation systems may be used in place of isopropanol.

Even more importantly, none of these references teaches the use of direct chromatogram comparison to identify quantitative differences between subject and control samples of subject and control biological materials. Without that advantageous feature of the present invention, this method would offer little commercial advantage, since that is the feature that permits automation of the chromatogram comparison and peak-difference identification process.

Equally important to note is that none of the cited references recognizes, addresses, or attempts to solve the problem solved by the present invention. None of the cited references provides any teaching or suggestion to select aqueous isopropanol to solve the problem of:

> optimizing the quantitative extraction of a maximal number of chemically dissimilar metabolite species in a single extraction step in such a manner that further fractionation of the resulting extract can achieve substantially, or nearly absolute, mutually exclusive partitioning of chemically dissimilar classes of metabolites into fractions containing species that are chemically similar to one another in accordance with their native chemical classes (i.e. without significant hydrolysis or other modification of the native species and without introduction of exogenous chemical species that impair further analysis thereof).

That is the problem solved by the present invention. That is that basis on which – the *sine qua non* by which – direct comparison of the chromatograms of the resulting extracts and/or fractions immediately produces identification of quantitative differences in metabolism between or among different or differently-treated cells and tissues.

As none of the cited references teach or suggest this problem, these features, or these advantages, Applicants submit that these reference fail to establish obviousness of the present invention (including Claims 1-9 and 18-20). Applicants therefore respectfully request that the Examiner reconsider final rejection of Claims 1-9 and 18-20 as unallowable, and remove this rejection of those Claims. However, in the event that this Response is found unpersuasive to that end, Applicants have canceled Claims 1-9 and 18-20 hereof.

Item 6. Applicants thank the Examiner for allowing Claims 9-16 and 21.

Item 2. The inventor's 1.132 Declaration submitted October 10, 2003 has been held insufficient to overcome the obviousness rejection(s) of Claims 1-8 and 18-20 because the showing of unexpected results is allegedly not commensurate in scope with the Claims.

However, Applicants submit that, for the following reasons, the Declaration, in light of the Examples of the present Application, provides more than adequate support for the use of the method for extraction and analysis of the billions of biological entities, cell, tissues, and materials within the scope of the claims. Applicants have reported results of the method for a variety of tissue and cell types, e.g.: eukaryotes (fresh leaves, dried seeds, yeast cells) and prokaryotes. As previously stated, these consistent reported results for such membrane-and-wall-bound cells and tissues accurately predict the method applies at least equally well to solely-membrane-bound cells and tissues (e.g., from animals).

Also as previously discussed, the present invention does not rely upon (unpredictable) biological properties of molecules, but (predictable) physical-chemical properties of molecules. Furthermore, all biological entities share, in spite of their differences in metabolism, the same chemical classes of metabolite compounds: carbohydrates and relatives (e.g., saccharides, sugar phosphates), hydrocarbons and relatives (e.g., lipids, carboxylic acids, alcohols, esters, purines, pyrimidines), polyamides and relatives (e.g., proteins, peptides), etc. The method of the present invention has been shown useful for all of these and other classes of compounds. The Declaration demonstrates that the selection of aqueous isopropanol solves the problem addressed by the invention and that the other solvents taught in the cited references do not do so. Therefore, the Declaration provides clear support for the entire scope of the Claims.

Applicants also note that, while methanol does extract a wide variety of metabolites, that solvent does not provide the solution offered by the present invention in that methanol extraction does not reliably permit direct chromatogram comparison to result in immediate identification of quantitative differences between subject and control biological materials. The reason for this is that methanol extracts spontaneously de-esterify biological compounds, thereby changing the chemical identity of biochemical species: e.g., esters become acids and alcohols, and at a variety of different rates. This means that fractionation of the resulting extracts does not permit the essentially mutually exclusive partitioning that is needed in order to allow reliable identification of quantitative differences by direct chromatogram comparison.

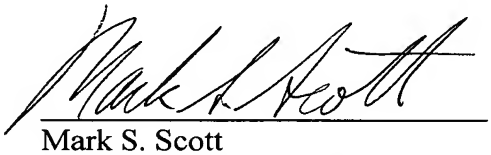
In light of the above remarks, Applicants submit that the inventor's Declaration does provide support commensurate in scope with the Claims (including Claims 1-9 and 18-20). Applicants therefore respectfully request that the Examiner reconsider final rejection of Claims 1-9 and 18-20 as unallowable, and remove this rejection of those Claims. However, in the event that this Response is found unpersuasive to that end, Applicants have canceled Claims 1-9 and 18-20 hereof.

CONCLUSION

Applicants believe that the above remarks and amendments overcome the objections and rejections presented in the December 30, 2003 Final Office Action. Applicants respectfully request that these objections and rejections be removed in light of these remarks and amendments, together with the teachings of the present Application and the noted inventor's Declaration. In any event, Applicants respectfully request allowance of the present Application.

Applicants request that if there are any issues remaining unresolved regarding any points raised by this Action, that an interview by telephone or in person be granted, to be arranged for a mutually convenient time. Reconsideration and allowance of the Application are requested in view of the above.

Respectfully submitted,



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